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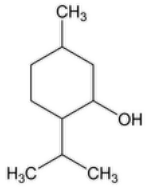
Menthol



$C_{10}H_{20}O$ 156.27

Cyclohexanol, 5-methyl-2-(1-methylethyl)- CAS RN®: 1490-04-6.

DEFINITION

Menthol is an alcohol obtained from oils derived from a variety of mints or prepared synthetically. Menthol may be levorotatory (*l*-menthol) from natural or synthetic sources, or racemic (*dl*-menthol). It contains NLT 98.0% and NMT 102.0% of menthol ($C_{10}H_{20}O$).

IDENTIFICATION

• **A.** The retention time of the major peak from the *Sample solution* corresponds to that of the menthol peak from the *Standard solution*, as obtained in the *Assay*.

• **B.** It meets the requirements in the test for *Optical Rotation*.

ASSAY

Change to read:

• **Procedure**

▲Internal standard solution: 10 mg/mL of 1-butanol in hexanes▲ (USP 1-Dec-2022)

Standard solution: 10 mg/mL of USP Menthol RS in ▲the *Internal standard solution*▲ (USP 1-Dec-2022)

Sample solution: 10 mg/mL of Menthol in ▲the *Internal standard solution*▲ (USP 1-Dec-2022)

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: GC

Detector: Flame ionization

Column: 0.18-mm × 20-m fused silica; coated with a 0.18-µm film of stationary phase G16

Temperatures

Injection port: 250°

Detector: 260°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
60	20	110	10

Carrier gas: Hydrogen

Flow rate: 0.9 mL/min

Injection volume: 0.5 µL

Injection type: Split ratio, 50:1

System suitability

Sample: *Standard solution*

▲[Note—The relative retention times for the internal standard and menthol are about 0.27 and 1.00, respectively.]▲ (USP 1-Dec-2022)

Suitability requirements

Relative standard deviation: NMT 2.0% for ▲the ratio of menthol to internal standard peak responses▲ (USP 1-Dec-2022) in replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of menthol ($C_{10}H_{20}O$) in the portion of Menthol taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak ▲response ratio▲ (USP 1-Dec-2022) of menthol ▲to the internal standard▲ (USP 1-Dec-2022) from the *Sample solution*

r_S = peak ▲response ratio▲ (USP 1-Dec-2022) of menthol ▲to the internal standard▲ (USP 1-Dec-2022) from the *Standard solution*

C_S = concentration of USP Menthol RS in the *Standard solution* (mg/mL)

C_U = concentration of Menthol in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Limit of Nonvolatile Residue**

Analysis: Evaporate 2 g, accurately weighed, in a tared open porcelain dish on a steam bath, and dry the residue at 105° for 1 h.

Acceptance criteria: NMT 0.05%

Change to read:

• **Related Compounds**

▲Internal standard solution,▲ (USP 1-Dec-2022) Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of each individual impurity in the portion of Menthol taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak area of each impurity from the *Sample solution*

r_T = sum of the peak areas from the *Sample solution*

Acceptance criteria

Individual impurities: NMT 0.5% for isomenthol (relative retention time is 1.08) from synthetic racemic menthol and 0.3% for all other impurities from natural and synthetic menthol

Total impurities: NMT 2.0%

• **Readily Oxidizable Substances in *dl*-Menthol**

Sample solution: Place 500 mg of *dl*-menthol in a clean, dry test tube. Add 10 mL of a solution of potassium permanganate, prepared by diluting 3 mL of 0.1 N potassium permanganate with water to 100 mL.

Analysis: Place the test tube in a beaker with water at a temperature between 45° and 50°. Remove the tube from the bath at intervals of 30 s, and mix quickly by shaking.

Acceptance criteria: The purple color of potassium permanganate is still apparent after 5 min.

SPECIFIC TESTS

• **Congealing Range of *dl*-Menthol**

(See *Congealing Temperature* ⟨651⟩.)

[Note—Perform this test preferably in a room with a temperature below 30° and a relative humidity below 50%.]

Sample: 10 g of *dl*-menthol, previously dried in a desiccator over silica gel for 24 h

Analysis: Place the *Sample* in a dry test tube with an internal diameter of 18–20 mm, and melt the contents at a temperature of about 40°. Suspend the test tube in water at a temperature of 23°–25°, and stir the contents of the tube continually with a thermometer, keeping the bulb of the thermometer immersed in the liquid.

Acceptance criteria: *dl*-Menthol congeals at a temperature between 27° and 28°. Shortly after the temperature has stabilized at the congealing point, add a few milligrams of dried *dl*-menthol to the congealed mass, and continue stirring. After a few min, the temperature of the mass quickly rises to 30.5°–32.0°.

• **Melting Range of *l*-Menthol**

(See *Melting Range or Temperature* ⟨741⟩.)

Acceptance criteria: 41°–44°

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 100 mg/mL in alcohol

Acceptance criteria

***l*-Menthol:** −45° to −51°

***dl*-Menthol:** −2° to +2°

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, preferably at controlled room temperature.
- **Labeling:** Label it to indicate whether it is levorotatory or racemic.
- **USP Reference Standards** ⟨11⟩

  USP Menthol RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MENTHOL	Nam-Cheol Kim Scientific Liaison	BDSHM2020 Botanical Dietary Supplements and Herbal Medicines

Chromatographic Database Information: Chromatographic Database

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